

REMARKS

Applicants respectfully request reconsideration of the present application in view of the foregoing amendments and in view of the reasons that follow. These amendments change and delete claims in this application. A detailed listing of all claims that are, or were, in the application, irrespective of whether the claim(s) remain under examination in the application, is presented, with an appropriate defined status identifier.

Claims 15, 17, 19, 21, 26, 28, and 30 are currently being amended. Claim 15 has been amended to refer to vector constructs carrying genomic fragments:

- (i) obtained from one or more pathogens;
- (ii) which have at least 80% homology to the genomic fragments of (i); or
- (iii) which are able to hybridize under stringent conditions to the genomic fragments of (i).

Support for sequences with at least 80% homology to the genomic fragments of (i) can be found at page 17, line 8, of the present application and support for sequences that are able to hybridize under stringent conditions can be found at page 17, lines 12 to 20. Claim 15 has also been amended to state that the vector constructs are selected from the group consisting of a plasmid comprising a genomic fragment between about 5 kilobases and about 25 kilobases and a cosmid comprising a genomic fragment between about 25 kilobases and about 50 kilobases. Support for such vectors and fragment sizes is found in original claims 17, 18, 26, and 27.

Claims 18 and 27 are requested to be cancelled, without prejudice or disclaimer thereof. No new claims are being added.

After amending the claims as set forth above, claims 15-17, 19-26, and 28-34 are pending in this application.

Because the foregoing amendments do not introduce new matter, entry thereof by the Examiner is respectfully requested.

35 U.S.C. § 112: Claims 15-17, 19-26, and 28-34 are Clear and Definite

Claims 15-34 are rejected under 35 U.S.C. 112, second paragraph, as being allegedly indefinite. Office Action at pages 2-3. Applicants respectfully traverse this ground for rejection.

Without acquiescing in the rejection and without intending to abandon claimed subject matter but to expedite allowance, claim 15 has been amended to further clarify the genomic fragments present in the constructs employed. Part (a) (ii) of claim 15 now refers to fragments which have at least 80% sequence identity to the fragment of (i) and part (a) (iii) refers to fragments which are able to hybridize under stringent conditions to the fragments of (i). Applicants have removed the objectionable term “derived” and therefore believe that the genomic fragments are clearly defined and claims 15-17, 19-26, and 28-34 are clear and definite. Withdrawal of this ground for rejection is respectfully requested.

35 U.S.C. § 112: Claims 15-17, 19-26, and 28-34 are Enabled

Claims 15-34 are rejected under 35 U.S.C. 112, first paragraph, as allegedly lacking enablement. Office Action at pages 3-5. Applicants respectfully traverse this ground for rejection.

Applicants address each aspect of the Examiner’s rejection under section 112, first paragraph, in turn.

(i) Genomic Fragments

As noted above, claim 15 has been amended to further clarify the genomic fragments that may be present in the vector constructs. The genomic fragments:

- (i) may be obtained from one or more pathogens;
- (ii) have at least 80% homology to the genomic fragment of (i); or
- (iii) may be able to hybridize under stringent conditions to the genomic fragments of (i).

The Examiner asserted on page 4 of the Office Action that “the scope of the claimed fragment reads on any virus cDNA, such as a HCV or HIV with a single mutation.” In other words, the Examiner alleged that claim 15 encompasses an entire viral genome with only one or two base changes that would be capable of reversion to cause an active viral infection. Claim 15 does not encompass such viruses with point mutations.

Claim 15 recites a core carrier with vector constructs carrying genomic DNA “fragments.” The skilled artisan would not interpret the term “fragment” to encompass an entire viral genome with only one or two base changes. Rather, one of ordinary skill in the art would consider an entire viral genome with one or two base changes to be simply a mutated virus, not a “fragment.” A “fragment” is a small piece of a whole thing and is not an entire genome with a few point mutations. Applicants submit with this response a definition of the term “fragment” from the Oxford English dictionary, which indicates that a fragment is:

“a small part broken off or detached”

See CONCISE OXFORD ENGLISH DICTIONARY 561 (Thumb Index Edition 2002).

Thus, a skilled artisan would interpret the phrase “genomic fragment” to mean a sub-region of a genome. He would not interpret it to mean a genome with only one or two base changes and certainly not one capable of spontaneous reversion. A small part of the whole is something missing a region and hence cannot simply revert because of the amount of the sequence that is missing. The presence of the term “fragment” means that the claims do not encompass such viruses. Accordingly, the full scope of claims 15-17, 19-26, and 28-34 is enabled.

(ii) Size of Fragments Accommodated by the Vector

The Examiner further asserts that “[a]ccording to the state of the art, not all plasmid or vector can carries [sic] more than 5 kb insert.” As mentioned above, to facilitate prosecution, claim 15 has been amended to refer to two specific types of vectors, namely plasmids and cosmids. In addition, upper and lower limits on the size of the genomic fragment present in the plasmids or cosmids have been inserted into claim 15. Thus, claim 15 refers to a plasmid

comprising a genomic fragment between about 5 to about 25 kb and a cosmid comprising a genomic fragment between about 25 kb to about 50 kb.

The insert sizes specified by claim 15 can be readily accommodated by plasmids and cosmids as highlighted at page 7, bottom paragraph of the present application. The Examples of the present application also exemplify both cosmids and plasmids carrying genomic fragments within the size ranges specified. The size ranges specified are therefore reasonable for cosmids and plasmids. Moreover, only vectors that can carry the recited genomic fragments are covered by the claims, because claim 15 recites that the vector constructs carry the genomic fragments. Accordingly, claims 15-17, 19-26, and 28-34 are both enabled and supported across the full breadth of the claims.

(iii) Core Carrier Composition

Finally, the Examiner asserts that the claims are not enabled because the “state of the art teaches that not all metal can be used as a antigen carrier protein because lots of metals are toxic as evidenced by de Boer JG et al. and Reid et al.” (citations omitted). de Boer JG *et al.* and Reid *et al.* do not suggest that a metal’s toxicity affects its ability to be coated with vector constructs. Accordingly, the Examiner has not shown why the full range of metals cannot operate as the core carrier according to the claims. Moreover, only metals that can be coated with vector constructs fall within the scope of the claims, because claim 15 recites that the core carrier is coated with vector constructs.

In addition, the toxicity of a metal is insignificant when metallic carrier particles are used for particle mediated transdermal delivery. In particular, the amount of metal utilized for any single administration is low; a large proportion of the carrier particles will simply be progressively shed from the skin; and there is no evidence that the metal from the carrier particles is systemically delivered to the subject. Indeed, toxicity of the type cited in the Official Action has not been seen when particle mediated delivery is utilized.

For instance, PowderMed’s own ND10 vaccine delivery device is currently designed to propel DNA (vaccine antigen)-laden microscopic (1-3 μm) metal particles into the

epidermis of the skin. Using traditional risk assessment terms and a log-order (worse-case of dose needed) quantity, epidermal administration of ten (10) vaccination units, for example, would theoretically deliver 200 µg metal/kg (*ppb*) to a standard reference body weight human (50 kg). From a risk assessment exposure perspective, it has been estimated that only 65% (6.5 mg) of the ND10 gas-entrained metal carrier particle payload penetrates the epidermis. Moreover, the majority of this “payload” (~90%, or 5.9 mg) has been shown to diminish over time with normal epidermal shedding (*i.e.*, 15-30 days, indicating a diminishing exposure), leaving the remainder (0.6 mg, or 12 *ppb*) to be processed by the phagocytic system. This is a very small portion of the original amount delivered.

Moreover, there is no evidence that the ND10-delivered metal is distributed systemically (histologic staining) and, hence, any effects are likely to be localized. Systemic toxicity, therefore, will not occur. Furthermore, the small amount of metal and the fact that the metal is in particulate form will also minimize any effects of the carrier particles on the subject.

The Official Action cites de Boer *et al.* (Carcinogenesis, 13(1):15-17 (1992)) and Reid *et al.* (Environ. Health Perspectives, 102 (suppl. 3) 57-61 (1994)) as indicating that under certain circumstances platinum, iron, and copper might be toxic. However, as discussed above, carrier particles, including platinum, iron, and copper, will be progressively sloughed off from the skin or disposed of by the phagocytic system. Accordingly, they are not dispersed systemically and are only delivered in relatively small amounts. Therefore, there will be no significant toxicity experienced by the subject and nothing that would render the use of such metals with particle mediated delivery unsuitable or cause any significant harm.

Thus, significant toxicity with such metals will not occur and particle mediated transdermal delivery is a safe and effective delivery route and any metal may be employed. Accordingly, the full scope of claims 15-17, 19-26, and 28-34 is enabled.

35 U.S.C. § 102: Claims 15-17, 19, 22-26, 28, and 31-34 are Novel

Claims 15-19, 22-28, and 31-34 are rejected under 35 U.S.C. 102(a) as being allegedly anticipated by Suter *et al.*, (Vaccine, 96(22): 12697-13702 (1999)). Office Action at pages 5-6. Applicants respectfully traverse this ground for rejection.

Suter *et al.* does not disclose a cosmid carrying a fragment of genomic nucleic acid that is between about 25 kb to about 50 kb in size or a plasmid carrying a fragment of genomic nucleic acid that is between about 5 kb to 25 kb in size.

As can be seen from the map of the vector employed in Suter *et al.*, fHSVΔpac, which is shown in Figure 1 of the article, the Herpes Simplex Virus ("HSV") sequences present in the vector are far in excess of the size limits specified by claim 15 of the present application. The non-HSV sequences present in Suter *et al.* are shown as a black box and represent a minimal portion of the construct. Thus, the amount of viral sequences present is well in excess of 100 kb and is in effect around 150 kb, in other words, virtually the entire HSV genome.

To illustrate this point, applicants submit a copy of Saeki *et al.* (Human Gene Therapy, 9:2787-2794 (1998)). This article provides additional details on the construction of fHSVΔpac. Figure 1(E) of Saeki *et al.* shows that the non-HSV sequences present in fHSVΔpac are only 4 kb long and confirms that the viral sequences are around 154 kb in length. Thus, the viral genomic sequences present in fHSVΔpac disclosed in Suter *et al.* are over 150 kb, as evidenced by Saeki *et al.* Accordingly, neither document discloses a plasmid or a cosmid with a fragment falling within the 5 to 25 kb and 25 to 50 kb ranges specified by claim 15 of the present application. The subject matter of claims 15-17, 19, 22-26, 28, and 31-34 is therefore novel over both documents.

35 U.S.C. § 103: Claims 15-17, 19-20, 22-26, 28-29, and 31-34 are Nonobvious

Claims 15-20, 22-29, and 31-34 are rejected under 35 U.S.C. 103(a) as being allegedly obvious in view of Suter *et al.* (Vaccine, 96(22): 12697-13702 (1999)) and Hilliard *et al.*

(Arch. Virol., 109(1-2):83-102 (1989)). Office Action at page 6. Applicants respectfully traverse this ground for rejection.

Neither Suter *et al.* nor Hilliard *et al.* disclose or suggest employing genomic fragments in immunization. These documents only direct one of ordinary skill in the art to employ modified *whole* viral genomes. There is no appreciation of employing a smaller region of the viral genome.

The claimed invention is based on the use of cosmids or plasmids carrying genomic fragments in immunization. The fragments in the vectors are not whole viral genomes, they are smaller subregions and, hence, cannot revert to give an active pathogen. The use of fragments, rather than the whole virus, has the further advantage that selected sets of antigens can be expressed, rather than all of the genes in the genome of the pathogen. This can be important because, as indicated at page 19, line 29, to page 20, line 2, of the present application, pathogens often express genes that down-regulate the immune response against the pathogen and, hence, it can be advantageous to deliver only a subset of genes rather than the whole pathogenic genome, including such modulatory sequences or other undesirable coding sequences.

Suter *et al.* is not concerned with the use of fragments of genomic DNA with the lengths specified by claim 15 in immunization. Instead, Suter *et al.* is concerned with a modified HSV genome containing virtually all of the viral genome and there is simply no appreciation of the possibility of using smaller fragments from the HSV genome in this document.

As highlighted in the abstract of Suter *et al.*, the construct employed, fHSVΔpac, contains a replication competent, but packaging defective, virus genome. The only modification to the entire HSV genome is to make three small deletions to remove the packaging sequences as illustrated in Figure 1 of Saeki *et al.* The construct fHSVΔpac still contains almost the entire HSV genome and over 154 kb of HSV sequences, including all of the HSV genes. The vector fHSVΔpac, therefore, mimics HSV infection, expressing all of

the HSV genes, producing cytopathic effects, and giving rise to viral particles. The only thing fHSVΔpac does not do, which HSV does do, is package its genome into the viral particles it produces, because of the deletion of the packaging sequences. Suter *et al.* therefore seeks to mimic infection with the whole virus.

There is simply no teaching or suggestion in Suter *et al.* to subdivide the HSV genome into smaller fragments of lengths about 5 to 25 kb and about 25 to 50 kb as specified by claim 15 of the present application. Instead, Suter *et al.* effectively adopts a disabled whole virus approach using a vector which can express every single HSV gene and imitate all of the other effects of HSV infection. There is no indication whatsoever in Suter *et al.* to subdivide the viral genome into smaller regions to express subsets of genes or any reason a skilled artisan would be motivated to generate such plasmid or cosmid constructs. Thus, nothing in Suter *et al.* would have led a person of ordinary skill in the art to subdivide the 150 kb HSV genome into much smaller 5 to 25 kb or 25 kb to 50 kb fragments as specified by claim 15. Suter *et al.* simply focuses on the expression of all of the HSV genes. As such the subject matter of claims 15-17, 19-20, 22-26, 28-29, and 31-34 is non-obvious over Suter *et al.*

Finally, Hilliard *et al.* adds nothing to the disclosure of Suter *et al.* Hilliard *et al.* simply compares HSV-1 to HSV-2. There is no appreciation of using a smaller fragment of a genome in immunization of the size lengths specified by claim 15. The subject matter of claims 15-17, 19-20, 22-26, 28-29, and 31-34 is therefore nonobvious over Suter *et al.* either alone or in combination with Hilliard *et al.*

Conclusion

The present application is now in condition for allowance. Favorable reconsideration of the application as amended is respectfully requested. The Examiner is invited to contact the undersigned by telephone if it is felt that a telephone interview would advance the prosecution of the present application.

The Commissioner is hereby authorized to charge any additional fees which may be required regarding this application under 37 C.F.R. §§ 1.16-1.17, or credit any overpayment,

to Deposit Account No. 19-0741. Should no proper payment be enclosed herewith, as by a check being in the wrong amount, unsigned, post-dated, otherwise improper or informal or even entirely missing, the Commissioner is authorized to charge the unpaid amount to Deposit Account No. 19-0741. If any extensions of time are needed for timely acceptance of papers submitted herewith, Applicants hereby petition for such extension under 37 C.F.R. § 1.136 and authorizes payment of any such extensions fees to Deposit Account No. 19-0741.

Respectfully submitted,

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fractional | Franco-

carnivorous mammal of the dog family with a muzzle, bushy tail, and typically a reddish coat (red fox) and other species. 2 informal a sly person. 3 N. Amer. informal a sexually attractive. 4 v. informal baffle or deceive.

fox foxlike adj.

fox of Gmc origin; rel. to Ger. *Fuchs*.

fox of the paper of old books or prints discoloured brown spots.

fox foxing n.

fox of Gmc origin; rel. to Ger. *Fuchs*.

fox a tall plant with erect spikes of typically purple flowers shaped like the fingers of gloves, *purple* and related species.

fox a hole in the ground used by troops as a point against enemy fire or as a firing point.

fox a dog of a smooth-haired breed, with ears, trained to hunt foxes in packs.

fox the sport of hunting a fox across country a pack of hounds by a group of people on foot.

fox fox-hunter n.

fox a reddish-brown moth with a velvety black caterpillar (*Macrotylus rubi*).

fox a common meadow grass with soft brush-like spikes (*Allopecurus pratensis* and related species).

fox a terrier of a short-haired or wire-haired originally used for unearthing foxes.

fox a ballroom dance having an uneven rhythm a code word representing the letter F, used in communication. 4 v. (-trotted, -trotting) dance.

fox 1 resembling or likened to a fox. 2 running or sly. 3 N. Amer. informal (of a woman) sexy. 4 (of wine) having a musky flavour (of other material) foxed.

fox foxily adv. foxiness n.

fox an entrance hall or other open area in a building, especially a hotel or theatre.

fox (denoting the centre of attention or activity) 'hearth, home'.

fox former pupils (especially in the name of some names).

fox 1 forte piano. 2 (f.p.) freezing point.

fox (in the UK) Family Planning Association.

fox Fellow of the Pharmaceutical Society of Britain.

fox (f.p.) abbrev. 1 feet per second. 2 foot-pound.

fox 3 frames per second.

fox Computing floating-point unit.

fox Father (as a courtesy title of priests). [from Fr. *frat* 'brother']

fox symbol. the chemical element francium.

fox a prefixed title given to an Italian monk or

fox Ital. abbrev. of *frate* 'brother'.

fox /frabdz/ adj. humorous delightful; joyous.

fox 1871: coined by Lewis Carroll, appar. to suggest joyous.

fox /frakz/ n. (pl. same /-kəz/ or US *fracas*) a disturbance or quarrel.

fox C18: Fr. from *fracasser*, from Ital. *fraccasso* 'to upbraid'.

fox /frakt(ə)l/ Mathematics n. a curve or geometrical each part of which has the same statistical characteristics the whole.

fox 2 a small or tiny part. 3 or fractal.

fox 1970s: from Fr. from L. *fract*, *frangere* 'break'.

fox /frak(ə)m/ n. 1 a numerical quantity that is whole number (e.g. 1/2, 0.5). 2 a small or tiny part. 3 or proportion. 4 a dissenting group within a one. 5 Chemistry each of the portions into which

mixture may be separated according to a physical property such as boiling point or solubility. 4 (usu. the *Fraction*) (in the Christian Church) the breaking of the Eucharistic bread.

fox ME: via OFr. from eccles. L. *fractio* 'breaking (bread)', from L. *frangere* 'to break'.

fractional adj. 1 of, relating to, or expressed as a fraction. 2 small or tiny in amount. 3 Chemistry relating to or denoting the separation of a mixture into fractions.

DERIVATIVES fractionally adv.

fractionize (also -ise) v. (usu. as adj. fractionalized) divide into separate groups or parts.

DERIVATIVES fractionalization n.

fractionate /frak(ə)neɪt/ v. chiefly Chemistry divide into fractions or components.

DERIVATIVES fractionation n.

fractions /frak(ə)ʃ(ə)nz/ adj. 1 easily irritated. 2 difficult to control.

DERIVATIVES fractionally adv. fractionousness n.

fox C17: from *fraction*, prob. on the pattern of the pair *fractio*, *fractio*.

fracture n. 1 the cracking or breaking of a hard object or material. 2 a crack or break, especially in a bone or a rock stratum. 3 the shape of the surface formed by a freshly broken rock or mineral. 4 Phonetics the replacement of a simple vowel by a diphthong owing to the influence of a following sound, typically a consonant. 5 v. break, or cause to break. 6 (of a group or organization) break up or fragment.

fox ME: from Fr. or from L. *fractura*, from *frangere* 'to break'.

fract /frækt/ prep. Scottish from.

fract N. Amer. military slang n. a hand grenade. 4 v. (fraggled, fraggling) deliberately kill (an unpopular officer) with a hand grenade.

fox C20: from *fragmentation* *grenade*.

fragile /fradʒaɪl/ adj. 1 easily broken or damaged. 2 delicate and vulnerable.

DERIVATIVES fragility n.

fox C15 (in the sense 'morally weak'): from L. *fragilis*, from *frangere* 'to break'.

fragile X syndrome n. Medicine an inherited mental disability resulting from an X chromosome that is abnormally susceptible to damage.

fragment n. /frægm(ə)nt/ a small part broken off or detached. 2 an isolated or incomplete part. 3 v. fragment /break or cause to break into fragments.

DERIVATIVES fragmental adj. (chiefly Geology) fragmentary adj. fragmentary adj. fragmentation n.

fox ME: from Fr. or from L. *fragmentum*, from *frangere* 'to break'.

fragmentation bomb (or fragmentation grenade) n. a bomb (or grenade) designed to break into small fragments as it explodes.

fragrance /frægr(ə)ns/ n. a pleasant, sweet smell. 2 a perfume or aftershave.

DERIVATIVES fragranced adj. fragrant n. (dated).

fragrant adj. having a pleasant or sweet smell.

DERIVATIVES fragrantly adv.

fox ME: from Fr. or from L. *fragrant*, *fragrans* 'smell sweet'.

frail adj. 1 weak and delicate. 2 easily damaged or broken. 3 n. US informal, dated a woman.

DERIVATIVES frailty n.

fox ME: from OFr. *fraille*, from L. *fragilis* (see *fractio*).

frailty n. (pl. -ties) the condition of being frail. 2 weakness in character or morals.

frail /frɛz, frɛz/ n. (pl. pronounced same) 1 (in cookery) a strawberry. 2 a white brandy distilled from strawberries.

fox ME: from Fr.

fraktur /fraktʃr/, German *fraktur* n. a German style of black-letter type.

fox C15: Ger. from L. *fractura* 'fracture' (because of its angularity).

frambesia /frambɛziə/ (US *frambesia*) n. another term for yaws.

fox C15: mod. L. from Fr. *framboise* 'raspberry', because of the red swellings caused by the disease.

framboise /frambwɔɪz/ n. 1 (in cookery) a raspberry. 2 a white brandy distilled from raspberries.

fox ME: from Fr.

frame n. 1 a rigid structure surrounding a picture, door, etc. 2 (frames) a metal or plastic structure holding the lenses of a pair of glasses. 3 the rigid supporting structure of a vehicle, aircraft, or other object. 4 a person's body with reference to its size or build. 5 a box-like structure of glass or plastic in which seeds or young plants are grown. 6 a basic underlying or supporting structure of a system, concept, or text. 7 Linguistics a structural environment within which a class of words or other linguistic units can be correctly used (e.g. I — him is a frame for a large class of transitive verbs).

fox a single complete picture, in a series forming a cinema, television, or video film. 8 the triangular structure for positioning the red balls in snooker. 9 a single game of snooker. 10 v. 1 place (a picture or photograph) in a frame. 2 surround so as to create a sharp or attractive image. 3 formulate. 4 a verb construct by fitting parts together or in accordance with a plan. 5 informal produce false incriminating evidence against (an innocent person).

fox be in (or out of) the frame be (or not be) eligible. 2 be wanted (or not wanted) by the police. frame of mind a particular mood.

DERIVATIVES frameable adj. framed adj. frameless adj. frame n. framing n.

fox OE *framian* 'to be useful', later 'prepare timber for building', 'make the wooden parts of a building': of Gmc origin and rel. to *fram*.

frame house n. chiefly N. Amer. a house constructed from a wooden skeleton covered with timber boards.

frame of reference n. 1 a set of criteria in relation to which judgements can be made. 2 a system of geometrical axes in relation to which size, position, or motion can be defined.

frame saw n. a saw with a thin blade kept rigid by being stretched in a frame.

frameset n. the frame and front fork of a bicycle.

frame tent n. chiefly Brit. a tent supported by a tall frame; giving it nearly perpendicular sides and standing head-room throughout.

frame-up n. informal a conspiracy to incriminate someone falsely.

framework n. an essential supporting or underlying structure.

franc /fræŋk/ n. the basic monetary unit of France, Belgium, Switzerland, Luxembourg, and several other countries, equal to 100 centimes (replaced in France, Belgium, and Luxembourg by the euro in 2002).

fox ME: from OFr. from L. *Francorum Rex* 'king of the Franks', the legend on gold coins struck in the 14th cent.

franchise /fræŋtʃ(ə)z/ n. 1 an authorization granted by a government or company to an individual or group enabling them to carry out specified commercial activities. 2 a business or service granted such authorization.

fox N. Amer. an authorization given by a professional league to own a sports team. 2 the right to vote in public elections, especially for members of parliament. 3 v. grant a franchise to. 4 grant a franchise for the sale of (goods) or the operation of (a service).

DERIVATIVES franchisee n. franchiser (also franchisor) n.

fox ME (denoting a grant of legal immunity): from OFr. based on *franc*, *franche* (see *frank*).

Franciscan /frænsɪsk(ə)n/ n. a monk, nun, or lay member of a Christian religious order following the rule of St Francis of Assisi. 2 adj. of St Francis or the Franciscans.

francium /frænsɪəm/ n. the chemical element of atomic number 87, an unstable radioactive member of the alkali metal group. (Symbol: Fr)

fox 1940s: from the country France + -ium.

franco- (also franco-) comb. form French; French and

sil | i | cosy | i: see | ɒ | hot | ɔ: saw | ʌ |

u | put | u: too | ʌ | my | ɔ: how | ex | day | ʊ | no | ɪ | near | ɔɪ | boy | ʊə | poor | ʌ | ɪ | fire | ɔ: | saw

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Concise Oxford ENGLISH Dictionary

THUMB INDEX EDITION



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